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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/839,073	04/20/2001	Todd C. Sacktor	13492	2721

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EXAMINER	
PAK, MICHAEL D	

ART UNIT	PAPER NUMBER
1646	

MAIL DATE	DELIVERY MODE
10/30/2009	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	09/839,073	SACKTOR, TODD C.	
	Examiner	Art Unit	
	Michael Pak	1646	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *19 June 2009*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *16-22* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *16-22* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *1-20-09*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Response to Amendment

1. Claims 16-22 are examined below. Claims 1-15 have been cancelled.

2. Applicant's arguments filed June 19, 2009, have been fully considered but they are not found persuasive.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

3. Claims 16-22 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a new matter rejection.

Claim 16 recite "wherein the synaptic transmission comprises long-term potentiation (LTP)" which is new matter because the specification does not disclose the claimed invention. The specification does not disclose the subgeneric claim limitation of a synaptic transmission comprising long term potentiation.

Claim 16 recite “effective to decrease synaptic transmission in said mammalian neuron” which is new matter because the specification does not disclose the claimed invention. The specification does not disclose the subgeneric claim limitation of decreasing synaptic transmissioin is mammalian neuron.

Claim 18 recite “the contacting of said neuron with with the inhibitor of PKMς is at the outer surface of said neuron, followed by the entry of said PKMς inhibitor into the cell” which is new matter because the specification does not disclose the claimed invention. The specification does not disclose the generic claim limitation cited but rather disclose the injection of the inhibitor.

Applicants argue that with figure 7 and page 9 of the specification one of ordinary skill in the art would know that an inhibitor of PKMzeta would be effective to decrease synaptic transmission where that synaptic transmission comprises LTP. Applicants argue that the specification states that PKMzeta is both necessary and and sufficient for the long-term maintenance of LTP. However, the specification does not disclose the claimed limitation of ““wherein the synaptic transmission comprises long-term potentiation (LTP)”. The figure 7 provides a specific example of a figure of voltage recording but does not provide example of “wherein the synaptic transmission comprises long-term potentiation (LTP)”.

Applicants argue that page 9 of the specification makes it clear that PKMzeta has arole in maintaining enhanced synaptic transmission with studies of LTP, conversely, inhibition of PKMzeta may cause amnesia. Applicants argue that one of ordinary skill in the art would know that if PKMzeta maintained enhanced synaptic transmission with

LTP, an inhibitor of PKMzeta would decrease synaptic transmission with LTP. However, one of ordinary skill in the art can speculate using logic what would be an extension of an invention but the specification has not disclosed the invention which is a subgeneric limitation of "effective to decrease synaptic transmission in said mammalian neuron".

Applicants argue that page 21 of the specification discusses diffusion of PKMzeta inhibitor into a target cell after exposure to PKMzeta inhibitor. However, page 21 of the specification discusses the purification of baculovirus expressed PKMzeta which does not disclose the subgeneric claim limitation of "effective to decrease synaptic transmission in said mammalian neuron".

4. Claims 16-22 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Applicant claims methods of decreasing neuronal synaptic transmission in a mammalian subject by administering inhibitor protein kinase M zeta (PKMζ). The examples taught in the specification demonstrate only injection of myristoylated pseudo substrate peptide of SEQ ID NO:4 and chelerythine inhibitor of PKMζ to whole cells in culture using a pipette. There is no actual demonstration that any animal has decreased neuronal synaptic transmission using the techniques disclosed, although the

specification teaches at page 14, lines 18-21 that the "principle active ingredient" can be administered at about 0.1 to about 10 nanomolar doses to achieve the desired results. There is no teaching that this amount is indeed necessary and sufficient to achieve decreased neuronal synaptic transmission in any animal. Since PKMζ must cross the blood-brain barrier to achieve its intended effect, there is no demonstration that applicant has achieved any form of a pharmaceutical preparation that would do so. In addition, it is unclear that the disclosed amounts would decrease neuronal synaptic tramsmission in an animal without causing serious unintended consequences. As noted by Oster et al. [Molecular Brain Research 127:79-88 (2004)], the PKCs (protein kinase C) family of if isozymes is complex, with many functions. It is noted at page 80, first column: "PKCs participate in a wide variety of physiological and pathophysiological processes in the brain and the whole organism. The question, however, of specific PKC participation in the different signaling pathways involved in these processes, is far from answered. The broadly overlapping substrate specificities and biochemical properties of the PKC isotypes in vitro, suggesting at least partial enzymatic redundancy in vivo, further complicate this challenge." Regarding PKMζ, Oster et al. state: "The PKMζ protein lacks all these autoinhibitory elements. In fact, once transcribed, the activity of PKMζ seems only to be regulated by protein degradation." Given that the PKMζ protein is only regulated by protein degradation, it is unclear what effect excessive amounts of inhibitor of PKMζ may have on physiological processes in the animal that receives this protein in a method to decrease neuronal synaptic transmission. Applicant's own post-filing reference published in 2002 using a Drospophila melanogaster transgenic fly

shows enhanced memory when the introduced mouse PKMζ gene was induced in vivo. See Drier et al. [Nature Neuroscience 5(4):316-324 (2002)]. This is not commensurate with administration of exogenous inhibitor of PKMζ, however, and the reference does not teach how one would accomplish decreased neuronal synaptic transmission by simply administering the PKMζ protein to an animal. Further complicating the predictability of applicant's claimed methods, applicant's own prior art published in 1998 demonstrates that transgenic mice with double the expression level of the PKMζ protein demonstrate not only "significantly reduced memory" but "show an increased frequency of neurofibromas." This teaching in the prior art would seriously question the enablement of administering inhibitor PKMζ protein to mice, and possibly all mammals for the purpose of decreasing the neuronal synaptic transmission. See Barad et al. [Society for Neuroscience Abstracts 24(1-2): p328, abstract no. 131.14 (1998)].

Furthermore, claims are drawn to decreasing synaptic transmission in all brain neurons and spinal cord neurons. However, the long term potentiation has been taught only in CA1 region of the brain. Thus it would require undue experimentation to discover all the neurons claimed which comprises long term potentiation characteristics.

Applicants argue that figure 2 and page 21 disclose the claimed invention. However, page 21 of the specification does not discuss the reduction in EPSC. Figure 2 teaches the use of hippocampal slices to measure voltage changes. The specification does not enable the administration claimed.

5. No claims are allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

6. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Michael Pak whose telephone number is 571-272-0879. The examiner can normally be reached on 8:00 - 2:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Nickol can be reached on 571-272-0835. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/Michael Pak/

Primary Examiner, Art Unit 1646